

was alive to every sensation, she particularly refers to the process of breaking up the adhesions of the right tumor, which she says were five, and the separation of which caused an indescribable measure of suffering.

In her after-treatment, she says that she had a doctor, or a student of medicine with her, night and day for several days, and thinks they felt her pulse every half-hour. She remembers being permitted to walk once across her room at the completion of two weeks; and taking a ride of two miles, a week later. She expressed to me in writing, a loving gratitude to Dr. Atlee for his faithful care and attention as her physician, and for his skill as the instrument in restoring her to perfect health. She has led a busy life for half a century, and is described as still "active and sprightly."

329 SOUTH TWELFTH ST., PHILADELPHIA.
November 14, 1893.

A CONTRIBUTION TO OUR KNOWLEDGE OF EPIDEMIC CEREBRO-SPINAL MENINGITIS.

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(Concluded from page 172.)

SYMPTOMATOLOGY.

REGARDING the symptomatology, we shall content ourselves with giving a very brief *résumé* of the notes taken, paying most attention to the symptoms most prominent in this epidemic. We shall lay especial stress upon certain of the clinical features (*e. g.*, the blood examination) which heretofore have been insufficiently studied. The peculiar conditions which obtain in an infectious intra-cranial disease are such as to render the clinical picture very complex. In local infections elsewhere in the body (*e. g.*, pneumonia, diphtheria) it is comparatively easy to separate clinically the symptoms and physical signs due to the local action of the infectious agent on the one hand from those dependent for their origin on the absorption and distant action of its toxic products. In diseases within the skull, however, more than anywhere else in the body, it is the size of the pathological new production and the quickness of its development which are of significance for the severity and course of the disease. Quincke has recently again emphasized the fact that even the simple serous accumulations within the skull-cavity, no matter where

they are situated, if sufficiently extensive, may produce the most severe symptoms, or even cause death.

In epidemic cerebro-spinal meningitis we have to think of the results which may follow, not only the more or less sudden outpouring of an exudate (cortical, basal, or intra-ventricular), but also those which are consequent upon the direct and remote action of the toxins which are produced by the micro-organisms, and we have to decide whether the lesions in distant organs (lungs, heart, joints) are to be looked upon as absorption-effects or as a localization of the same organism in these parts, or as complicating infections due to other bacteria. As Leyden has pointed out, the gravity lies more often in the evil effects of the exudation on the functions of the brain than in the severity of the infection; if the meningitis be cortical, epileptiform convulsions endanger life; if there be marked exudation into the ventricles, then coma and brain paralysis too often ensue.

From what we have said, and from the results of pathological examinations, the complexity of the question becomes easily evident, and an attempt to analyze the different disturbances in function, and to connect each definitely with its pathological basis would seem at first to be well nigh hopeless. Nevertheless, with the constant acquisition of facts and better methods of technique, we need not despair of finally arriving at a position in which we shall be able to cope more or less successfully with these problems.

It was possible at Lonaconing to make out most of the different types of the affection which have been described—fulminating, acute, subacute, intermittent, and abortive. The onset of the disease was, in the majority of the cases, sudden, the individual being attacked without warning with severe headache and vomiting, symptoms which were often followed in a few hours by delirium, stiffness and retraction of the neck, and severe constitutional disturbances. In only a few cases was there a definite recognizable prodromal stage, with general malaise, headache, and dragging pains in the limbs.

Compared with other epidemics, the number of fulminating cases (*cas foudroyants*) was large, no less than ten patients dying within forty eight hours after seizure, one child indeed succumbing in eight and another in ten hours after the appearance of the first symptoms. In the less violent but still severe cases the symptoms lasted from six to fourteen days, when either death occurred or signs of slow improvement ensued. Many abortive cases were observed in which, after a sudden onset, with perhaps severe symptoms, the patients recovered with striking rapidity.

Several cases of the "intermittent type" occurred during this epidemic, and in these periods of comparative well-being alternated with marked exacerbations. The convalescence was often tedious, and the danger was by no means over when the acute symptoms had subsided.

Even after there was good reason to believe that the causative bacteria were all dead and convalescence seemed to be established, serious symptoms would reappear, which would suggest that as long as the exudate is not completely reabsorbed there is danger.

The symptoms in general, we may say, presented no regularity. The disease is full of surprises, and the clinical phenomena of one day or hour may differ greatly from those of the next.

Especially inconstant was the course of the fever, and the temperature charts are interesting, chiefly in that they show that no fixed type of pyrexia can be definitely assigned to this disease. Nor did the height of the fever bear any relation to the severity of the other symptoms; the sudden and often marked elevations and depressions of the temperature independent of general symptoms could be explained only by assuming a direct interference with the functions of the thermo-regulatory centres. Even the absence of pyrexia did not permit the making of a favorable prognosis.

The other symptoms referable to disturbances of the central nervous system, the headache, the vertigo, the delirium, the paralysis of the eye-muscles, the deafness, the general hyperæsthesia, and the twitchings showed almost as great irregularity as did the temperature curve.

Among the clinical appearances noted which were due to lesions of the cranial nerves and their centres in the different cases may be mentioned anosmia, strabismus (almost always divergent), nystagmus (usually horizontal or vertical), inequality of pupils, photophobia, ptosis, defects of vision, facial rigidity, trismus, slowed respiration, Cheyne-Stokes breathing, deafness and disturbances of speech.

On account of its rarity, it is interesting to record one case in which we observed definite rotary nystagmus. The patient was a girl of seventeen, who had severe general symptoms with distinct evidence of a basal exudate. During a part of one day the left eyeball was rotated definitely in its socket, the excursions apparently corresponding to the limits of the movements of rotation. On reviewing the literature, we have been able to find reference to only one similar instance—a case mentioned by Jaffé.

The intra ocular changes have been especially studied in this epidemic by Dr. R. L. Randolph. Out of thirty-five cases in which he examined the fundus, it was normal only in seven. The most frequent alteration was passive congestion in the retinal veins, with congestion of the optic disks. In several cases there was a distinct optic neuritis, and in one instance the central vein was thrombosed.

The retraction of the neck was very commonly present; in some cases the occiput was drawn well back between the scapulæ. The thighs and legs were frequently flexed, but extreme opisthotonos was not often seen. There was general hyperæsthesia of the skin, and attempts to change the

position of a patient gave rise to severe pain. In the graver cases there were marked twitchings of the muscles and tendons, and in some, especially a short time before death, convulsions and coma.

The tendon reflexes varied much, but in many cases were diminished, which is to be attributed, no doubt, to the extent of the interference with the posterior roots of the spinal nerves.

Beyond the nervous arrhythmia, the respiratory organs were not markedly implicated, and it was only rarely that one met with an associated bronchitis or broncho-pneumonia. General cyanosis was not uncommon. A very frequent feature in the epidemic was epistaxis, a symptom which does not seem to have often attracted the attention of observers elsewhere.

The pulse was sometimes slowed, sometimes accelerated, and often intermittent. Beyond the blowing systolic murmurs so frequently heard over the cardiac area in children in febrile affections, there were very few symptoms referable to the heart or pericardium.

The lips, teeth, and tongue were covered with *sordes*, especially in the graver and more protracted cases. A few patients showed mild anginas, and the tonsillar crypts were not infrequently filled with white cheesy-looking plugs. The chief symptom pertaining to the digestive system was the vomiting, which, in some cases, was persistent and intractable, leading to inanition and emaciation. Where the retraction of the neck was great there was often difficulty in swallowing; in some cases the dysphagia appeared to be due to interference with the normal innervation. The bowels were, as a rule, constipated, although diarrhœa occasionally occurred. Indeed, in four cases a well-marked dysentery was observed, the feces containing mucus, pus, and blood. Occasionally in a grave case there would be incontinence both of the urine and the feces.

In one case of dysentery the feces were carefully examined. The reaction was found to be alkaline, the odor very foul, and mucus, pus, and blood were visible to the naked eye. A fresh specimen of the mucopurulent portion, examined microscopically, showed, besides the epithelium from the surface of the mucous membrane, many round cells of variable size, which were often fatty and vacuolated. Some of these were certainly polynuclear leucocytes, others resembled rather lymphoid cells. In the protoplasm of several cells which had the size of polynuclear leucocytes, besides large vacuoles, one could make out single included cells of small size. Red blood-corpuscles were also present. Smear cover-glass preparations, dried and stained in various ways, showed as the predominating organism lancet-shaped cocci in pairs, apparently encapsulated. In addition, there were slender bacilli, a few shorter, thicker bacilli (resembling *B. coli communis*), and short chains of streptococci. It must be mentioned that in the two cases which came

to autopsy large lumbricoid worms were found in the alimentary canal, and, on inquiry, we learned that they had been observed in many of the cases, both in the vomit and in the feces.

The spleen was at times slightly enlarged, as shown by percussion; the splenic dulness, however, did not pass beyond the costo-articular line, and in no instance was the border of this organ palpated. Abdominal retraction was not a prominent symptom on the whole. The only symptom referable to the liver was the occurrence of mild jaundice in two of the cases.

The cutaneous changes were widely divergent. Many of the cases ran their course without any apparent exanthem, and if one were to be guided only by the majority of cases in this epidemic he would be compelled to discard the name "spotted fever" for the disease. Herpes was very common, and formed an early and important symptom. It was situated chiefly on the lips, nose, ears, and neck following the distribution of the cutaneous vessels and nerves. Purpuric and petechial eruptions were seen in a comparatively small proportion of the patients; one of the commonest forms of eruptions was an indistinct purplish mottling over the surface of the body, which appeared and disappeared almost under the eyes.

The urine varied in amount in different cases and in different stages of the disease. As a rule it was concentrated, but occasionally a patient would pass large quantities having a low specific gravity. In the severer cases, and especially in those running an acute course with high fever, slight albuminuria was common, and microscopical examination of the sediment showed the presence of hyaline and granular casts. Erlich's diazo-reaction was negative in every case in which it was applied. The reaction has, however, been present in the urine in a few instances in meningitis, but only according to Ehrlich in very severe cases. The urine contained an excess of phosphates, a point to which several observers, notably v. Grimm, have called attention. In many cases there was a white precipitate of triple phosphates equal to one third or more of the volume of urine passed. In none of the specimens examined could the presence of sugar be demonstrated.

THE JOINTS.—Nearly twenty per cent. of the severe cases suffered from complicating joint affections, the knees being most frequently attacked, the elbows, wrist, and ankle following in frequency in the order named. The effusions were peri-articular as well as intra-articular, and the joints were swollen and reddened, resembling closely those of acute articular rheumatism. Indeed, there were cases which, had it not been for certain initial symptoms indicating a meningeal process, could easily have been diagnosed as nothing more than attacks of rheumatism. Similar cases have been noted in other epidemics, and there are references in the literature which draw attention to the prevalence

of meningitis and of rheumatism in the same community at the same time.¹

Speaking generally, it may be said that for this epidemic at least, complications in the joints occurred more frequently in the better class of patients, and it is interesting to note that the meningeal symptoms appeared to be favorably influenced by their appearance.

Kernig, of St. Petersburg, has described a symptom which he believes to be pathognomonic of meningitis. In thirteen cases he observed a peculiar flexion-contracture (*Beuge-kontraktur*) of the knee-joints which could not be reduced when the patient was in the sitting position. In attempting to extend the knee, the leg could not be straightened further than a point where it made an angle of about 135° with the thigh, although when lying or standing this contracture was completely absent. If the patient lay on his side with the thighs drawn up the symptom was still present. It has been claimed that the same phenomena may be seen in many other conditions (old age, chronic alcoholism, etc.), but Kernig asserts that he has examined thousands of individuals with particular reference to this point, and has never found this contracture except in cases of meningitis. Unfortunately we were not familiar with this suggestion when at Lonaconing, and so cannot say anything as to the value of "Kernig's symptom."

THE CONDITION OF THE BLOOD.—There have been very few opportunities for studying the blood in cases of epidemic cerebro-spinal meningitis since the more general employment of the finer methods of hæmatological technique; and in the literature we have been able to find only meagre references to the subject by Halla, v. Limbeck, and Rieder. The two former found a leucocytosis in cases of suppurative meningitis, while Rieder observed two cases of epidemic cerebro-spinal meningitis, one having 20,100 white corpuscles, the other 17,500 to the cubic millimetre. We were fortunately able to examine the blood of

¹ These facts are, we think, not without importance as bearing upon the etiology of acute rheumatism. There can be little doubt, it seems to us, although for the proof we must look to cultural experiments, that in the joint complications in epidemic meningitis, the articular and the peri-articular inflammations are due to local infections with the same bacterium which has set up the meningitis. Moreover, in at least one case of genuine acute rheumatism the micrococcus lanceolatus has been isolated in pure culture from the joint effusion, and Foa and Bordoni-Uffreduzzi have been able to set up a polyarthritis in rabbits by subcutaneous inoculation of this diplococcus. The frequent association of rheumatism with endocarditis, and with inflammation of the pleura, pericardium, and peritoneum lend support to the view that at any rate in a certain proportion of the cases the pneumococcus may be the cause. Nevertheless it is probable that acute articular rheumatism will, ere long, be proven to have no *etiological unity*, just as has already been proven for the inflammations of the serous membranes generally. It seems probable that the entrance of pyogenic organisms of different varieties into the circulation, under circumstances which are inconsistent with the development of the phenomena of a general septicæmia, may give rise to inflammations in some one or more of the serous membranes of the body—be it meninges, pleura, pericardium, peritoneum, or joint surface, the particular ones attacked depending on certain peculiarities either in the virulence of the invading organism or in the lessened resistance at the moment of the serous membrane implicated.

several of the cases at Lonaconing, but shall include in this report only a few typical examples.

In order to avoid error, every precaution was taken in these examinations. The blood in all cases was taken with the aid of a sterile lancet from the lobule of the ear, previously thoroughly cleansed with alcohol and ether. The blood was examined fresh in each case, care being taken to secure specimens which spread out into a layer of only one corpuscle in thickness. These were examined immediately with an oil immersion lens. The hæmoglobin was estimated by the instrument of v. Fleischl. The readings were made in a dark room, with artificial light, and through a cylinder of paper some twelve inches in length. Moreover, the readings were made by two individuals, and where the results differed at all the mean of the readings was recorded. By this method of control any gross error was avoided. For the enumeration of the corpuscles the blood-counter of Thoma-Zeiss was employed, the methyl-violet solution of Toison being used as a diluting fluid. Finally coverslips were prepared for drying and staining by the methods of Ehrlich. For this purpose particular care was taken to secure good specimens, and on subsequent examination all imperfect preparations were discarded. We shall epitomize the results of our examinations. In the fresh blood slide no marked variations in size or shape of the red corpuscles could be made out; in some of the cases, however, there was distinct pallor of the red cells. The increase in the number of the leucocytes was quite evident in many cases in the examination of the fresh drop of blood, and a greater number of white corpuscles appeared to be motile than one sees under normal conditions. Many of the leucocytes presented a striking vacuolation, a condition which, we believe, is not uncommon in the leucocytes dependent on other causes. The blood-platelets were present in clumps, but did not appear to be decidedly increased or diminished in numbers.

As to the number of corpuscles present, the average of a number of counts shows that a diminution of the red cells is not a marked feature of the disease. In some of the advanced cases, with emaciation there was a moderate oligocythæmia, but in the majority of instances the full complement of red blood-corpuscles was present. The hæmoglobin, however, in all cases examined was somewhat diminished in amount, so that the individual corpuscular holding in hæmoglobin (*valeur globulaire*) was below par. A well-marked leucocytosis is, we believe, a constant phenomenon in the disease during its active stages. In no case examined, except in convalescent patients, was it absent. The number of white corpuscles varied in different cases in our experience, between 12,000 and 32,000 to the cubic millimetre. That the degree of variance is greater, however, there can be little doubt, and it is probable that further investigations will prove that still larger leucocytoses may exist, especially in cases of meningitis associated with complications in the lungs or joints. The dried specimens were fixed by heating for an hour and a half on a copper bar at 120° C., and then stained, some of them in solutions of eosin and methylene-blue, some in the triple stain of methylene-green, acid fuchsin and orange green.

In none of these specimens were micro-organisms found, although they were patiently looked for. The "color analysis" of the leucocytes

showed in every case the increased number of white blood-corpuscles to be due to an increase in the cells with neutrophilic granules and polymorphous nuclei. The mononuclear cells (small and large) were relatively diminished in number. It will be seen that these changes in the blood are not peculiar to meningitis, but are quite in accord with the leucocytoses associated with suppurative inflammations, or inflammations accompanied by well-marked local exudation anywhere in the body.

As examples the following four cases may be cited:

Bessie B. (Case XVII. of Dr. Porter's series), aged four years, always healthy before; had been a bright, stout, well-nourished girl. One evening in the last week in January felt cold and chilly, and had distinct rigor during the night, followed by vomiting and severe pain in the head. During first week she was very restless, had muscular hyperæsthesia, inequality of pupils, rapid pulse, and uttered a sharp cry from time to time. Two purpuric spots appeared on buttocks. Retraction of the neck began about the eighth day. Up to this time the patient ate and drank well, and appeared rational. The mother now noted that the child could not use the right arm, and on examination it was found rigid and swollen. Herpetic eruption appeared about the tenth day.

Note dictated February 14: Child lies on left side, moderately emaciated, legs drawn up, thighs flexed, right arm rigid, resists movement; head retracted; whole body held stiff and rigid; attempts to move the child cause her to cry out; face slightly mottled and has a bluish tint; lips bluish-red and covered with sordes; remains of herpetic eruption visible. Tongue grayish-yellow, moist coating thicker in the centre than at the edges; pupils even, midway between contraction and dilatation. No ocular paralyses; veins in forehead rather prominent; thorax symmetrical; expansion equal; marked pulsation in vessels of neck; resonance clear throughout front, axillæ, and back; a few whistling rhonchi heard at bases. Pulse equal at the two wrists, 18 to the quarter, very irregular and arrhythmical. Sometimes there would be two or three beats of varying intensity followed by a pause corresponding to the time of from two to four beats; volume of pulse rather small. Apex beat of heart in fourth interspace 1 cm. inside the left nipple line. Dulness not increased; loud blowing systolic murmur heard over whole cardiac area, greatest intensity at the third left interspace 1 cm. from sternal margin. Pulmonic second sound relatively accentuated. Splenic dulness begins at the eighth rib and extends to the costal margin; does not pass the costo-articular line. Border not palpable, possibly owing to rigidity of abdomen. Liver dulness begins at the seventh rib in right mamillary line and extends to costal margin; border not palpable. Skin dry, no œdema; no marked change in tendon reflexes; no lymphatic enlargement.

The blood examination was made on February 14. Even in the fresh drop of blood the increase in the white elements could easily be made out. The count showed 4,448,000 red and 24,000 white blood-corpuscles; hæmoglobin, 72 per cent. Dried and stained preparations showed a marked increase in the number of polynuclear leucocytes with ϵ -granules, and a relative diminution in the number of lymphocytes and large mononuclear leucocytes.

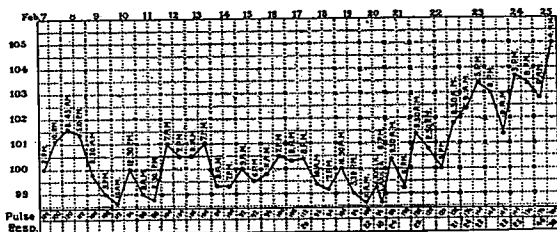
Florence D., aged sixteen years. The onset in this case had been gradual, the patient having pain in the head and back for several days before any serious symptoms appeared. On January 29, at 1 P.M., she had a severe chill followed by excruciating pain in the head, causing loud shrieks and restlessness; this was associated with vomiting and excitement. Next day

the patient was decidedly deaf and more or less stupid. Later she became delirious, and often had to be held in bed. She picked her nose from time to time and had several attacks of epistaxis. Distinct purpuric eruption appeared on face and neck and a few spots on body. None of them were very bright and none of them turned yellow or green afterward. During part of her illness she had retention of urine and had to be catheterized. Her bowels were constipated. Spleen and liver not distinctly enlarged. The temperature never went higher than 103.5°. She had marked eye symptoms, including divergent squint, paralysis of accommodation, and nystagmus. On ophthalmoscopic examination there was a definite optic neuritis in the right eye (Dr. Randolph). The girl died at the end of the third week of the disease. Toward the end she was much cyanosed and showed well-marked Cheyne-Stokes respiration. Her urine was examined several times and found to contain a trace of albumin and numerous hyaline and granular casts.

The blood was examined on two successive days in the third week. As the results of the two examinations were practically the same, we give that made on February 15. In the fresh blood slide, the examination of two or three fields sufficed to show that the leucocytes were distinctly increased in number. The vacuolation of the leucocytes was especially striking in this case. Hæmoglobin (v. Fleischl), 45 per cent. Blood-count: red blood-corpuscles, 4,896,000; white blood corpuscles, 24,500. The dried and stained specimens showed a marked relative increase (over 85 per cent.) in the neutrophils with polymorphous nuclei, and a relative decrease in the different mononuclear forms. Several typical normoblasts seen.

Agnes S., aged nine years, taken ill on February 7, 1893. Complaining of chill, severe pain in the head, and vomiting. The temperature, as will

FIG. 4.



be seen by referring to the accompanying chart, was not high at the beginning. There was severe pain in the neck and inability to move muscles of limbs on account of pain. No marked retraction of neck. She continued with comparatively mild symptoms for some ten days when, on February 17, she had diarrhoea, cramp-like pains in the abdomen, with a little blood and mucus in the stools. These symptoms were relieved the next day, but on the 18th she suffered from extreme pain in left ear, requiring morphine for its relief. On the 20th it was noticed that she had no power in right arm and leg, and there was some incontinence of urine and feces. Paralysis of right side of face. On 23d temperature rose to 101.8°. Next day well-marked evidence of complicating bronchitis and broncho-pneumonia.

Pulse and respiration became more rapid and temperature higher. Death on evening of February 25. Temperature, 105°; pulse estimated at over 200.

The blood examination in this case was made on February 14th. In the fresh blood slide the increase in the white elements was easily demonstrable. Marked vacuolation of the leucocytes. Hæmoglobin (von Fleischl) 72 per cent. Blood-count, red blood-corpuscles 5,032,000; white corpuscles 29,500. Cover-glass preparations from this case dried and stained in the "triple stain," gave the following "differential count" of white elements:

		Per cent.	Proportions in normal blood.
			Per cent.
Small mononuclear	53	4.9	15 to 25
Large mononuclear and transition forms	74	6.8	4 to 6
Neutrophiles with polymorphous nuclei	946	87.3	70 to 75
Eosinophiles	0	0.0	1 to 5
Myelocytes	10	1.0	
Total number counted	1093	100.0	

Only one nucleated red blood-corpuscle (typical normoblast) seen in the whole slide.

In making the differential counts it was thought best to adopt the simple classification given above rather than the more complicated one of Uskow. According to the suggestion of Thayer, we have made the counts so that the small mononuclear elements correspond to the small and large lymphocytes, the small transparent forms and some of the smaller transitional forms of Uskow; the large mononuclear and transitional forms including all other non-granulated forms, with the exception of transparent polynuclear leucocytes. In terms of Uskow's classification the characteristic change in these leucocytoses consists of an increase in the *ripe*, and especially in the *over-ripe* elements with a relative decrease in the number of the *young* or *unripe* elements.

The complete absence of leucocytes with eosinophilic granules did not hold for the other cases examined. The number of typical myelocytes seen in this case was rather striking, and, had the patient been an adult, would perhaps have been of considerable pathological significance. In the blood of children, however, one often sees, even under normal conditions, a variable number (nearly always, however, under 1 per cent.) of these cells.

For comparison, we give the results of a differential color analysis of the blood taken from a woman, thirty-eight years of age, who had suffered from a prolonged attack of meningitis, and had a moderate leucocytosis:

	Per cent.
Small mononuclear elements	10.9
Large mononuclear and transition forms	2.1
Eosinophiles	0.6
Neutrophiles with polymorphous nuclei	86.4
Myelocytes	0.0
	100.0

Lizzie L., aged fifteen years (service of Dr. Skilling), was seen during convalescence. She had suffered from a severe attack, the temperature at the beginning reaching nearly 105°. There had been retraction of the neck and delirium for some four or five days, and excessive vomiting. Abundant

herpatic eruption on lips, cheeks, hands, and wrists, the discoloration still remained. Marked constipation at first. No paralysis, no joint complications, no tenderness below neck. Had been sitting up the day before blood examination was made.

In the fresh blood-slide the red corpuscles were noticed to be distinctly paler than normal. No apparent increase in number of white elements. Hæmoglobin 55 per cent. Red blood-corpuscles, 5,004,000. White blood corpuscles, 9000. In the dried and stained specimens the different varieties of leucocytes were present in about normal proportions, the over-ripe (multinuclear) elements being still, however, slightly in excess. A few typical normoblasts seen. This count is given in that it shows the disappearance of the leucocytosis with the advent of convalescence.

TABLE.

Patient.	Age.	Attending physician.	Day of disease.	Temperature at time of examination.	Hæmoglobin (v. Fleischl).	Red blood-corpuscles to c.mm.	Valeur globulaire.	White blood-corpuscles to c.mm.	W. R.	Remarks.
					p. ct.					
B. B.	4	Dr. Porter	17th	...	74	4,448,000	0.84	24,000	1:185	Dysentery as a complication.
F. D.	16	Dr. Porter	18th	101.2°	45	4,896,000	0.47	24,500	1:199	Albumin and casts in urine.
A. S.	9	Dr. Porter	7th	100.5	72	5,032,000	0.7	29,500	1:170	
L. L.	15	Dr. Skillings	...	99.2	55	5,004,000	0.55	9,000	1:556	Convalescent.

A word of explanation is necessary with regard to the low percentage of hæmoglobin found in the blood of Florence D. and Lizzie L. Both these girls showed clinically a decided pallor of the skin and mucous membranes, although as the blood-counts show the red corpuscles were present in nearly normal numbers. The marked diminution in the *valeur globulaire*, taken with the age and sex of the patients, made us think of a pre-existing chlorosis, and on inquiry we learned that both had been noticed to be slightly pale for some months previous, and that both had complained of more or less constipation and certain menstrual irregularities. It is almost certain, therefore, that the low percentage of hæmoglobin observed in these two cases was not entirely dependent upon the meningeal inflammation.

And finally, in this connection, it will not be out of place, in view of the many interesting observations which have been made regarding the bearing of the presence or absence of a leucocytosis in diseases due to the lanceolate diplococci (acute lobar pneumonia, pneumococcus-infections in rabbits) upon the severity of a given infection and upon the prognosis, to state that, in the fatal cases which we have had the opportunity of examining during life the presence of a leucocytosis was always demonstrable. While for confirmation of this point it will be necessary to study many more cases in future epidemics, yet the evidence, as far as it goes, is in favor of the view which we have already mentioned, that death

in cerebro-spinal meningitis results from the local intra-cranial mischief, rather than from the infection *per se*.

The death-rate at Lonaconing corresponded to that of an epidemic of moderate severity, about 40 per cent. of the cases (excluding those classed as abortive) proving fatal. Hirsch, in his monograph, states that out of 15,632 cases 37 per cent. died. v. Ziemssen placed the mortality of mild epidemics at 20 per cent., and of the severest epidemics at 70 per cent.

PATHOGENESIS.

The disease, then, being known to be due, at least in the majority of instances, to the action of a specific micro-organism, viz., the micrococcus lanceolatus, we have next to consider by what mode the infectious agent gains entrance to the body, and more particularly into the meninges of the brain and cord, and in what way, if at all, it is thrown off. Again we have to inquire whether, if it can be thrown off, it will ever then be in a condition to infect other individuals.

Unfortunately a wholly satisfactory answer cannot at this time be given to these questions. We are not yet in possession of sufficient data based on a close study of the epidemiology and bacteriology of the disease, to enable us to more than indicate the probable mode of infection and the conditions which predispose to the origin and propagation of the disease.

The simultaneous prevalence of other infectious diseases in the localities in which epidemic cerebro-spinal meningitis existed, has been held to be of some significance. The occurrence of pneumonia at such times must be regarded as of special importance, for, as we have said, the same infectious agent is the cause of both diseases, and in the epidemic of cerebro-spinal meningitis studied by Foà and Bordoni-Uffreduzzi the most of the cases were complicated by pneumonia. Epidemic parotitis has been noted as occurring in a community in connection with or just before the outbreak of this disease. Parotitis was epidemic at Lonaconing at the time of the prevalence of meningitis, and we may remark that there are in the literature references which go to show that the micrococcus lanceolatus may be the cause of this disease also.

Again, other infectious diseases, scarlet fever, measles, typhoid fever, influenza, and coryza, have been mentioned by different writers as concomitant epidemics.

While in pneumonia, and probably a certain number of cases of parotitis and coryza, the same organism as that found in meningitis is known to occur, yet in the other infectious diseases mentioned, the infectious agent, so far at least as is known at present, is in none of them the micrococcus lanceolatus. Moreover, it is to be remembered that meningitis does not attack by preference those suffering or just recovering from other infectious diseases, if we exclude pneumonia. These diseases occur as concomitants or as precursors only.

Hence it is clear that in the search for predisposing factors we must look further than the infectious diseases with which epidemic meningitis may coexist. And it is not improbable that we shall find that, although one disease does not depend upon the other for its development, yet the same conditions of life which permit one to flourish may also engender the other.

It has been suggested by Strümpell that there may be some relation between coryza and epidemic meningitis. This, he thinks probable, on account of the observations of Weigert, that in some cases of the disease there is a purulent inflammation of the nasal sinuses. Weichselbaum found in some of his cases of meningitis purulent inflammation of the nasal and sphenoidal sinuses and the middle ear, and in all these he demonstrated diplococci. One must, we think, hesitate before accepting it as even highly probable that the majority of cases originate in this way. On the other hand, a sharp line of distinction must be drawn between those cases which are definitely primary and those which are secondary. There are, undoubtedly, cases in which there has been an extension of disease in the middle ear to the meninges, and why should not the same thing happen in diseases of the nasal sinuses? Such cases may simulate the sporadic form of the disease. But what is necessary is to see whether or not cases associated with diseases of the middle ear and those of the nasal mucous membrane occur in such numbers during an epidemic as to make this mode of origin the probable one in all. In the acute case in which we performed an autopsy no disease of the nasal sinuses existed.

With our present knowledge it seems more probable that we have to do with an infection by the way of the blood current rather than by continuity from the nose or ear. The common occurrence of meningitis in pneumonia indicates the possibility as well as the frequency of this mode of infection. In those cases in which pneumonia does not occur, other sources of entrance for the infectious agent must be sought; and to this category belongs especially the epidemic form. In any consideration of this subject at the present time, infection from the nasal¹ and oral cavities, in the latter case by lymphatic communication, as suggested by Ortmann, is a possibility which cannot safely be rejected. Nevertheless, the writers have been led to believe that the intestinal tract may be regarded as the way of entrance into the blood-current, if not in all, at least in many of the cases.

In two of the cases which we observed clinically, and which afterward proved fatal, there was dysentery. Cultures and cover-slip preparations were made from the evacuations of one of these, and the predominating

¹ The lymphatics of the mucous membrane of the nose can be injected from the sub-archnoidal lymph space (Schwalbe, Key, and Retzius.)

organism present was the micrococcus lanceolatus. In both of the cases which came to autopsy there was enteritis. And in other epidemics the occurrence of dysentery has been noted. Yet constipation as a feature of the disease is of more common occurrence than diarrhoea. This may be considered at first as militating against the conception of the intestinal tract as the place of entrance into the body of the infectious agent. But it is perfectly conceivable that the organisms may enter through the intestinal canal without first producing a demonstrable lesion therein, and find in the meninges of the central nervous system a *locus minoris resistentiæ*. The case of meningitis, as reported by Ortmann as due to the micrococcus lanceolatus secondary to typhoid fever is important as indicating the possibility of entrance from the intestine. Here, however, undoubted lesions of the mucous membrane were present.

Owing to the slight vitality of the organism in acid media, and as the intestine must become invaded after the infectious material has first passed through the stomach, it is necessary to draw attention to one point that may be of significance. Whether in all the persons attacked there is an alteration in the gastric juice by which its acidity is either diminished or altogether abolished, we cannot say, as we were unable to obtain the contents of the stomach from a number of cases. But in the vomit obtained from one child sick of the disease, free hydrochloric acid was demonstrated to be absent. Still, were this not the rule, there are periods in health during the fasting hours, when the stomach is free, or nearly so, from acid contents. In this connection the observations of Ewald are full of interest. He found that when water was introduced into the stomach a small amount passed immediately into the intestine; after about an hour the rest went suddenly over into the duodenum, and this part had no acid reaction, so that any bacteria present were not subjected to the harmful influence of an acid medium. Flügge has recently emphasized this point when dealing with the method of spread of cholera through drinking-water. In our disease the diplococci are of course not necessarily in the water imbibed, but in the process of swallowing it is easy to understand how they could be washed from the mouth and throat (their constant habitat), and so gain entrance to the stomach, and finally to the intestines uninjured.

The importance of considering the intestine as a probable infection-atrrium in epidemic cerebro-spinal meningitis becomes evident when it is remembered that about 80 per cent., and according to some authors (Kruse and Pansini) 100 per cent., of all persons in health carry about constantly in their mouths the micrococcus lanceolatus, and according to Netter, in 20 per cent. of these the organisms possess sufficient virulence to kill animals when injected into them. This fact removes the necessity of searching for the infectious agent outside the body, in, for example, the soil or the water.

Most writers on the subject now agree that the disease is not contagious, but is rather of "miasmatic" origin. The localization of the infectious agent in the closed cavity of the central nervous system certainly does not favor the infection of the surroundings. Still in some epidemics, that in Hamburg for example, the disease was known to appear in a locality in which it previously existed, but from which it had disappeared; and the interval of time which had elapsed was in some instances considerable. These facts would seem at first to be irreconcilable with the view that there is no infection of locality. We have shown that an organism possessing the culture and morphological properties of the micrococcus lanceolatus is thrown off with the dejections in some cases of cerebro-spinal meningitis, and as indicated by the experiments of Bordoni-Uffreduzzi, Guarnieri, Netter, Patella, Nikiforoff, Sirena, and Alessi, and Kruse and Pansini, the organisms may retain their vitality and even virulence when dried in sputum, blood, etc., sometimes for four months. Hence we are not at this time justified in excluding the possibility of the infection of locality. This assumption seems, however, in view of the wide distribution of the organism in nature, to be hardly necessary. It is, we think, more probable, that the local conditions which enabled the first cases to appear, persisting, other susceptible individuals are attacked, so that fresh cases appear in the site of the previous ones, in fact that we have to do with a "predisposition of community" rather than an "infection of locality."

If we are then to believe that the disease is, in the majority of instances, the result of an auto-infection, and this would be equally true whether we conceive it to be due to the entrance of the bacteria from the nose or pharynx or from the intestinal canal, it still remains for us to determine the nature of the unusual conditions which render the system vulnerable to the invasion of the micro-organism, and what it is that brings about the localization by preference of the morbid process in the cerebro-spinal meninges.

When excluding air, water, soil and food, as carriers of the infectious agent, we by no means intend to deny that they may play an important rôle in the causation of the disease. And concerning Lonaconing, the local conditions are such as would naturally produce a lessening of the powers of resistance of a number of individuals, and thus render them, although apparently in good health, susceptible to the disease. While in this epidemic, as we have already said, the more prosperous classes were by no means exempt, it was chiefly the poor that suffered, and the disease prevailed particularly in localities in which the houses were close together, and in which overcrowding existed, with the attendant evils of unsanitary arrangements, improper and insufficient food, and unclean bedding and clothing.

Nevertheless, although the facts pointed to a predisposition of the

whole community outside the merely personal predisposition, in the end the resistance of the tissues of each individual must necessarily be of prime importance in determining infection or immunity.

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THE TIMES AND MODES OF THE INTRODUCTION OF THE EXOTIC DISEASES OF CHILDREN INTO AMERICA.¹

By J. LEWIS SMITH, M.D.

THE tribes of American Indians occupying North and South America, left to themselves, have never, so far as I am aware, made any important or effective effort to improve their condition. When the Europeans discovered America the chief endeavor of the Indian was to obtain shelter from the weather by rudely constructed huts, to appease hunger by vegetables of spontaneous growth, or by the products of hunting and fishing, and to repel the encroachments of neighboring warlike tribes by implements scarcely better than those of the stone age. Their diseases were chiefly such as are due to climactic influences, such as pertain to the normal growth and decay of the body and to the disturbance of its functions.

The medical literature of America, at least that of North America and in the English tongue, was very meagre during the two centuries succeeding the discovery of America. But there is, I think, sufficient historical evidence that the highly contagious and fatal diseases of infancy and childhood, which to a great degree check the increase of population in both hemispheres, were unknown to the American Indian until communicated by the European.

First we will consider those two loathsome diseases² of a vicious and dissolute life, diseases which now prevail among the profligate in all countries reached by commerce and travel. These two diseases were not differentiated from each other until long after the discovery of America. Though described in text-books as diseases of adults, they not infrequently affect children in one way or another. Inherited syphilis is likely to be fatal in infancy unless properly treated, and in those who survive it is a common cause of scrofula or deterioration of

¹ Address at the opening of the Pediatric Section of the Pan-American Medical Congress.

² Syphilis and gonorrhoea.